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REPLY

We thank Dr. Cheng for his interest in our work (1) and appreciate his comments. The prevalence of hypertrophic cardiomyopathy (HCM) appears similar among different racial groups. Population studies comprising more than 16,000 subjects from Japan, China, and the U.S. (Caucasian, African, and native Americans) have established that unexplained left ventricular (LV) wall thickness ≥ 15 mm occurs with a prevalence of about 0.2% (range 0.16% to 0.23%) (2–5). Recent genotype–phenotype studies have revealed that the disease expression of HCM is extremely heterogeneous and that many gene carriers present with electrocardiographic (ECG) abnormalities in the absence of LV hypertrophy on echocardiography. It is likely, therefore, that the true prevalence of HCM is well above 0.2% (1). Furthermore, the prevalence of HCM appeared to be similar in each of the screening studies despite considerable age differences in the study populations, which suggests that HCM may develop independent of age. This finding is in contrast to previous assumptions that HCM develops during adolescence and early adulthood. If this was the case, the prevalence would be age-dependent and expected to be high at young ages and low at older ages owing to increased mortality rates associated with HCM. Apparently, the number of individuals dying equals the number of individuals developing the condition at any age, resulting in a “steady-state” and age-independent prevalence of the condition.

The frequency of mutations in the gene for cardiac troponin I (*TNNI3*) has been reported in six larger studies (6–9). A total of 1,697 HCM patients have been investigated (range: 71 to 748 patients), with an average frequency of *TNNI3* mutations of 2.7% (range 0.9% to 4.0%). The studies were conducted in patients in Great Britain, the U.S., France, China, Japan, Korea, and Germany. The modest differences in frequency of mutations are most likely explained by differences in sample sizes of patients and do not appear to be associated with race.

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doi:10.1016/j.jacc.2005.04.009

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Impact of Carvedilol Before Angiotensin-Converting Enzyme Inhibitor Therapy on Cardiac Function

The study by Sliwa et al. (1) is indeed an eye-opener for those who depend on expert opinions such as those from the American College of Cardiology/American Heart Association guidelines (1,2). However, despite a well-executed study, I am not sure the conclusions drawn by the editor and investigators are entirely on the mark. My main criticism is that this is a “how-to” treat and not a “what to” treat study, and as a result it cannot ignore practicality issues. In clinical practice, how often do we see 78 consecutive newly diagnosed patients with New York Heart Association (NYHA) functional classification II to IV go directly to oral anticongestive therapy without the need for parenteral vasodilator intervention initially? In these patients, is it really practical to switch directly from parenteral therapy to oral beta-blockade without the support of an afterload reducing agent? Even among specialists, a measurable dropout rate would be expected if every patient went straight to a beta-blocker. In fact, the concept of using an inodilator to facilitate the commencement of a beta-blocker in those patients who would otherwise not tolerate adrenaline withdrawal or inhibition is for this very reason.

Conversely, concerning the control arm, are there many practitioners who would wait six months before introducing a beta-blocker? Therefore, I am surprised the researchers did not elaborate on the treatment status of the subjects before they were randomized to the carvedilol arm, and whether they encountered difficulties during up-titration. Furthermore, as a significant number of subjects expired during the study (11 of 78, 14% after 12 months), how many required readmission for decompensation and what happened to their beta-blocker dosing regimen?

As for the results, improved biochemical profile, NYHA functional class, and echocardiographic function in the carvedilol-initiated group would indicate that carvedilol is a more “potent”